Attorney Docket No: 37637-0003

In re patent application of

Rainer HINTSCHE *et al.*

Serial No.: 09/142,660

Group Art Unit: 1655

Filed: December 23, 1998

Examiner: B. Sisson

For: DETECTION OF MOLECULES AND MOLECULE COMPLEXES

REPLY UNDER 37 C.F.R. § 1.116

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants herein respond to the Office Action mailed September 18, 2001 (Paper No. 32). Please debit any underpayments, or credit any overpayments, to firm deposit account no. 08-1641.

REMARKS

Claims 21-55 and 58-61 are pending and stand finally rejected. Reconsideration of the claims and withdrawal of each rejection are earnestly solicited in view of the following remarks.

Rejection under 35 U.S.C. § 112, first paragraph:

A. Background

Only one issue remains in the instant application; namely, the rejection of claims 21-55 and 58-61 as allegedly non-enabled under 35 U.S.C. 112, first paragraph. Applicants thank Examiner Sisson for conducting a telephonic interview with Applicants' representative on October 24, 2001. During the interview, an overview of the law of enablement, as well as potentially allowable subject matter in this case, were discussed. For the reasons cited below, Applicants maintain that the claims satisfy the requirements of 35 U.S.C. § 112, first paragraph.

In one aspect, the invention concerns a method of detecting a molecule or molecule complex in a diluent, solvent or gel, which includes the steps of: contacting the molecule or molecule complex with an ultra-microelectrode array that contains at least two electrode structures, wherein the spacing between the electrode structures is less than 3 μm; producing an alternating electric field between the electrode structures; and measuring changes in current or potential between the electrode structures, whereby the changes in current or potential are caused by the molecule or the molecule complex. In a particular embodiment, the spacing between the electrode structures is less than 1 μm.

B. The PTO attempted, but failed, to make a *prima facie* case of non-enablement

The Examiner raised the enablement issue in the Office Actions dated December 8, 1999 (Paper No. 8), and August 1, 2000 (Paper No. 13), contending that the specification does not teach one of ordinary skill in the art how to make and use the full scope of the claimed invention. The Office Action dated September 18, 2001 (Paper No. 32) maintains the enablement rejection. While Paper Nos. 13 and 32 recite the eight *In re Wands* factors, the Office Actions do not list any credible, objective evidence to cast doubt on the claims' presumption of validity. *See* MPEP § 2164.04. For instance, the Examiner reasons that the "[I]llustrative embodiment," provided at pages 13-14 of the Specification, is insufficient to satisfy the enablement requirement. The illustrative embodiment describes the detection of β-galactosidase-streptavidin, by utilizing methods of the invention.

The record is, however, devoid of any objective reasoning to as to why the lack of multiple working examples renders the claimed invention defective under 35 U.S.C. § 112, first paragraph. This is significant in that the MPEP makes clear that working examples are not *per se* required to satisfy the enablement requirement. *See* MPEP § 2164.02; *see also Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). Furthermore, the foregoing

standard, requiring a reasonable basis to question the enablement provided for the claimed invention, is applicable "even when there is no evidence in the record of operability without undue experimentation beyond the disclosed embodiments." MPEP § 2164.04 (citing *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).[1]

The Examiner relies upon U.S. Patent No. 5,200,313 ("the '313 patent") as evidence that the disclosure does not delineate certain steps that need to be taken in order to practice the claimed invention. *See* Paper No. 8 at 7-8. The '313 patent does not, however, support the Examiner's position. First, the '313 patent merely lists certain factors (*e.g.*, the nine factors listed in Paper No. 8, *id.*) that may be considered in developing a hybridization protocol. The '313 patent does not state, however, that all hybridization reactions are unpredictable. Second, the '313 patent became part of the public record at least as early as April 6, 1993 (issue date); and the disclosure issuing as the '313 patent was written at least as early as March 1, 1985 (filing date of the parent, a "continuation" application).[2]

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[1] Here, there is evidence in the record of operability without undue experimentation beyond the disclosed embodiments. *See, e.g.*, Appendix B of the Second Declaration.

[2] The application issuing as the '313 patent is a continuation of application Ser. No. 707,420, filed Mar. 1, 1985, now abandoned, which is both a continuation-in-part of application Ser. No. 616,132, filed Jun. 1, 1984, now abandoned, and a continuation-in-part of application Ser. No. 626,927, filed Jul. 9, 1984 is now abandoned, which is a continuation-in-part of application Ser. No. 520,524, filed Aug. 5, 1983, now abandoned.

The present application, on the other hand, has an international (PCT) filing date of March 12, 1997—many years subsequent to the relevant dates of the '313 patent. Indeed, the '313 patent actually supports Applicants' position that the claims satisfy the enablement requirement, since the nine factors that the Examiner cites are part of the "state of the art." *See* MPEP § 2164.05(a) (stating that the Examiner is supposed to consider "[t]he state of the art existing at the filing date of the application ... to determine whether a particular disclosure is enabling..." Based on the foregoing, Applicants maintain that the Examiner has not posited a *prima facie* case of non-enablement.

C. The objective evidence Applicants supplied in response to the PTO's arguments further supports Applicants' position that the claims satisfy the enablement requirement

Despite the PTO's shortcomings in substantiating a *prima facie* case of non-enablement, Applicants nonetheless supplied objective evidence to further illustrate that the claimed invention is enabled. In this regard, Applicants submitted the declarations of inventor Rainer Hintsche ("Dr. Hintsche") filed pursuant to 37 C.F.R. § 1.132 on December 29, 2000 ("the First Declaration") and August 27, 2001 ("the Second Declaration").

In the First Declaration, Dr. Hintsche explained, *inter alia*, that the experimentation necessary to determine specific variables for detecting different molecules would be routine to the skilled artisan in the field of the present invention. *See id.* at ¶ 2B. To support this statement, the First Declaration noted, "employees of Fraunhofer Gesellschaft and working in the Institute of Silicon Technology... have proved that the present invention can be carried out for the detection of molecules different than those described in the examples in the application..." *Id.* at ¶ 2C. The First Declaration also reports of Dr. Hintsche's disclosure to the "5th World Congress on Biosensors" that the instant Application enabled skilled workers to detect DNA hybridization, as well as differences between "full-matching," "mismatching" and "no-matching." *Id.* at ¶ 2D. The First Declaration further cites scientific articles co-authored by the named inventors, which disclose additional instances of practicing the invention beyond the scope of the "[i]llustrative embodiment." *See id.*

The Second Declaration, which is a source of yet additional objective evidence, corroborates Dr. Hintsche's attestations in the First Declaration. For example, the Second Declaration discloses "post-filing" data as evidence that one of ordinary skill in the art could—by using the teachings of the specification in conjunction with the knowledge in the state of the art at the Application's effective

filing date—practice the claimed invention far beyond the embodiments explicitly set forth in the Specification. In particular, the Second Declaration highlights four occasions where skilled workers in the art were able to detect nucleic acid molecules and polypeptides in accordance with the claimed invention. *See id.* at ¶ ¶ 7 and 9 (citing Appendix B attached thereto). The steps set forth in these post-filing examples are taught by the Specification and/or are well known to skilled workers in the art, as evidenced by the parenthetical citations at each step. *See id.* at Appendix. B.

By presenting the foregoing evidence in the form of the First and Second Declarations, Applicants shifted the burden to the Examiner to weigh all the evidence before him, "including... any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled." MPEP § 2164.05 (emphasis added). It is noted that "[t]he evidence provided by applicant need not be conclusive but merely convincing to one skilled in the art." *Id.*

D. The PTO has not properly considered the evidence Applicants submitted in the First and Second Declarations

It appears, however, that the Examiner has not properly considered Applicants' objective evidence, as required by MPEP § 2164.05. *See* Final Office

Action dated September 18, 2001 (Paper No. 32). Although the September 18, 2001 Office Action contains a section entitled, "Response to Arguments," it appears that the Examiner has not analyzed Applicants' evidence in the manner prescribed by the MPEP and the Court of Appeals for the Federal Circuit. The Examiner's maintenance of the enablement rejection in the absence of a fair consideration of Applicants' evidence is legal error.

1. The Declarations must be given due consideration, even though the Declarant in each instance is a named inventor

The dismissal of the evidence on the grounds that "the declarants are also the inventors and as such have a vested interest in the outcome of the examination of the subject application" (Paper No. 32 at 7, lines 7-8) is improper. Applicants endeavored to proffer objective evidence, *e.g.*, post-filing data obtained by utilizing only the teachings of the specification, supplemented by conventionally available art, to further illustrate why the claims satisfy 35 U.S.C. § 112, first paragraph. The Declarations cannot, therefore, be dismissed as espousing nothing more than self-serving or conclusory statements. *See In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) ("expert's opinion on the ultimate legal conclusion must be supported by something more than a conclusory statement").

2. In an enablement analysis, it is improper as a matter of law to limit the "state of the art" to art cited in the specification

The MPEP requires an examiner to consider "[t]he state of the art existing at the filing date of the application ... to determine whether a particular disclosure is enabling..." MPEP § 2164.05(a). Since the "state of the art" cannot be completely depicted in one document (*i.e.*, a patent application), it is improper to limit the state of the art to the "four corners" of the Application. As the Court of Appeals for the Federal Circuit ("Federal Circuit") noted in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, a specification need not disclose what is well known in the art. 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986).

Yet, the analysis provided in the September 18, 2001 Office Action does not adopt this standard. For instance, the Examiner states, "[a] review of the disclosure of the subject application does not find that these prior art publications [cited in the post-filing working examples] were relied upon for enablement." *Id.* at 8, lines 12-14 (emphasis added). By confining the enablement analysis to the four corners of the Specification, the Examiner has, in effect, failed to "consider" any of the evidence cited in the Second Declaration, and much of the evidence submitted in the First Declaration, which violates MPEP §§ 2164.05 and 2164.05(a). Therefore, the Examiner's conclusion at page 8, lines 14-15 that "[t]he examples... are not commensurate in scope with the disclosure of the

subject application" is ill founded, as it fails to give any weight to the conventional art cited in these examples. Accordingly, withdrawal of the rejection is solicited.

3. The PTO's reliance on *Genentech, Inc. v. Novo Nordisk A/S* is not well founded, as that case presented a fact pattern distinct to the facts in the extant Application

The Federal Circuit's analysis in *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997) does not support the Examiner's position. In *Genentech*, the issue was whether the specification, at the time of filing, would have enabled one of ordinary skill in the art to use "cleavable fusion expression" to make human growth hormone ("hGH") without "undue experimentation," when the specification disclosed the DNA sequence encoding hGH. *Id.* at 1004. There, both the plaintiff (patentee) and the defendant (alleged infringer) agreed that the specification, itself, failed to describe how to make hGH using cleavable fusion expression. *See id.* (emphasis added). However, the patentee, Genentech, argued that a skilled worker in the field, upon combining (i) the disclosed DNA sequence encoding hGH with (ii) prior art cleavable fusion expression techniques applied to non-human proteins, would have been able to make hGH via cleavable fusion expression. *See id.*

The prior art relied upon by Genentech, however, was deficient in teaching one of ordinary skill in the art to make hGH through cleavable fusion expression. *See id.* For example, the enzyme (trypsin) that Genentech cited as enabling cleavable fusion expression of hGH was not known to possess this property at the time of filing. *See id.* Trypsin, instead, was known only as being capable of protein digestion—which is distinct to the biological property of specifically and precisely cleaving conjugate proteins. *See id.* Furthermore, the prior art cited by Genentech taught away from using trypsin to produce hGH via cleavable fusion expression. *See id.*

In other words, in *Genentech*, there was no way to piece together the prior art with the teachings of Genentech's specification to arrive at the claimed invention, because, *e.g.*, skilled workers in the field were not aware of enzymes suitable for carrying out cleavable fusion expression in human proteins. The court agreed, also noting that "no one had been able to produce any human protein via cleavable fusion expression as of the application date… [even though] DNAs encoding desirable human proteins were known at the time of filing." *Id.* at 1006. The court, accordingly, held that the claims did not satisfy the enablement requirement. *See id.* at 1007.

In the instant Application, however, the illustrative embodiment at pages 13-14 is evidence that skilled workers in the field were able to practice subject matter within the scope of the claims. Furthermore, the prior art cited, for instance, in the First and Second Declarations, does not act to supply the "novel aspects" of the invention, which was the case in *Genentech*. *Id.* at 1005. The cited references instead provide known techniques (*e.g.*, coating chips electrodes with DNA, configuring hybridization conditions, performing impedance measurements) that are used in effectuating the claimed methods. *See*, *e.g.*, Second Declaration at ¶ ¶ 9(a)(i) and (ii).

The facts in this situation are, on a whole, different from those of the *Genentech* case. Moreover, unlike in *Genentech*, the record in this case does not contain any objective evidence that casts reasonable doubt that the claimed invention would not be enabled. Accordingly, the *Genentech* holding is inapposite to the instant case; and withdrawal of the rejection is solicited.

CONCLUSION:

In view of the foregoing, Applicants respectfully request the Examiner to withdraw the rejection and pass the claims on to allowance. The Examiner is invited to contact the undersigned attorney to resolve any issues, in order to expedite the prosecution of the application.

Respectfully submitted,

December 17, 2001
Date

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